General

Guideline Title

Update of the clinical practice guideline for the management of rheumatoid arthritis in Spain.

Bibliographic Source(s)

GUIPCAR Group. Update of the clinical practice guideline for the management of rheumatoid arthritis in Spain. Madrid (Spain): Spanish Society of Rheumatology; 2011 Dec. 367 p.

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: GUIPCAR Group. Clinical practice guideline for the management of rheumatoid arthritis in Spain. Madrid: Spanish Society of Rheumatology; 2007 Mar. 301 p. [1260 references]

Recommendations

Major Recommendations

Definitions for the level of evidence (1-5) and the grades of recommendations (A-D) are sourced or provided at the end of the "Major Recommendations."

Diagnosis

Suspected Rheumatoid Arthritis (RA)

Importance of Early Diagnosis in RA

- The sooner RA treatment begins, the higher the likelihood of controlling the inflammatory process and reducing structural damage; thus, "recent-onset arthritis" should be considered a diagnostic priority. [1.a, A]

Detection of RA in Primary Care

- The longest a patient with suspected RA should wait for a rheumatology appointment is 2 weeks. [5, D]

Criteria for Referral to from Primary Care to Rheumatology

- All cases of arthritis lasting more than 4 weeks should be referred to specialty care, regardless of the suspected diagnosis. Patients with suspected septic arthritis should be referred immediately. [5, D]

Table: Criteria for Referral of Recent-Onset Arthritis to Specialty Care

Criteria for arthritis referral from the SERAP* project Presence during >4 weeks of:
1. Swelling in two or more joints, as evidenced by the squeeze test (lateral compression of metacarpophalangeal or metatarsophalangeal joints) 2. Involvement of metacarpophalangeal or metatarsophalangeal joints 3. Morning stiffness lasting more than 30 minutes
Specific rheumatoid arthritis (RA) referral criteria according to Emery
1. Swelling in three or more joints 2. Pain on palpating metacarpophalangeal or metatarsophalangeal joints 3. Morning stiffness lasting more than 30 minutes

*The SERAP project was launched in November 2004 by the SER (Spanish Society of Rheumatology) in 36 reference hospitals with rheumatology departments.

How to Improve Referral from Primary Care to Rheumatology Care

- The diagnostic yield from primary care can be improved if patients are discussed previously with the specialty unit or reference rheumatologist and/or with joint development of protocols defining the criteria for referral. [5, D]

Organization of the Consult in Its Interaction with Primary Care

- Training measures and protocols should be agreed with primary care physicians, with good communication between the two levels (primary and specialty care); this makes it possible to evaluate the effectiveness of the protocols, be reminded of the importance of using them, and demonstrate their utility. [5, D]

1987 American College of Rheumatology (ACR) Classification Criteria

- The 1987 ACR criteria have good sensitivity and specificity for the classification of previously established RA.
- The 1987 ACR criteria in list form (see Table below) perform well in patients with established disease. RA is considered to be probable when four or more of the seven criteria in the list are present. This diagnostic classification has a sensitivity ranging between 75% and 95%, and a specificity of 73% – 95%.
- The 1987 ACR classification criteria are currently widely used as the gold standard for RA diagnosis.
- The 1987 ACR criteria perform more poorly in disease of recent onset. In this stage the clinical criteria (1 to 4) are sensitive but not very specific for RA, while the remaining criteria are specific but not very sensitive.

Table: American College of Rheumatology (ACR) Classification Criteria for Rheumatoid Arthritis (1987)

1. Morning stiffness	Morning joint stiffness lasting at least 1 hour.
2. Arthritis of three or more joint areas	Simultaneous inflammation of at least 3 joint areas, as observed by a physician. The 14 joint areas are: proximal interphalanges, metacarpophalanges, wrists, elbows, knees, ankles, and metatarsophalanges.
3. Arthritis of hand joints	Inflammation of at least one hand area (carpal, metacarpophalangeal, proximal, interphalangeal).
4. Symmetrical arthritis	Simultaneous involvement of the same joint areas (as defined in criterion 2) on both sides of the body.
5. Rheumatoid nodules	Subcutaneous nodules over bony prominences, extensor surfaces, or in juxta-articular regions, observed by a physician.

6. Serum rheumatoid factor	Demonstration of elevated amounts of serum rheumatoid factor by any method for which the result has been positive in less than 5% of control subjects.
7. Radiologic changes	Radiologic changes typical of rheumatoid arthritis on posteroanterior hand radiographs. Must include erosions or unequivocal juxta-articular osteoporosis in involved joints.

ACR/EULAR Classification Criteria

- The main reason for drafting new criteria was the lack of sensitivity of the previous criteria (1987) in early disease.
- The objective was not to create diagnostic criteria or a referral tool for general physicians, but to develop new classification criteria to facilitate the study of patients in early stages of the disease.

Diagnostic Utility of Biological Tests in Recent-Onset RA

Anti-Cyclic Citrullinated Peptide Antibody (Anti-CCP)

- Anti-CCP determination should be requested when evaluating a patient with recent-onset arthritis. [1b, A]

Evaluation

Specific RA Evaluation

Appropriate Data for First Evaluation of RA Patient

- The first evaluation of an RA patient should include: clinical history, physical examination, blood test, and urinalysis. [5, D]

Clinical History

- The clinical history should include: family and personal history, sociodemographic data, previous history of current disease and treatments (previous and concomitant). [5, D]

Physical Examination

- The physical examination, in addition to the routine exam of organs and systems, should include a detailed evaluation of the musculoskeletal system. [5, D]

Blood Test and Urinalysis

- The blood test should include: complete blood count, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), rheumatoid factor (RF), anti-CCP, liver biochemistry and serology, and renal function. For urine, a basic urinalysis is sufficient. [5, D]

Data Common to the Initial Evaluation and Follow-up of RA

- Both the initial and follow-up RA evaluations should be based on the systematic assessment of a minimum set of parameters which allow evaluation of the degree of inflammatory activity, functional disability, and residual structural damage. The use of specific forms to facilitate systematic data collection is recommended. [5, D]

Table. Minimum Set of Parameters for Rheumatoid Arthritis (RA) Evaluation Recommended by OMERACT 1993 (Outcome Measures in Rheumatoid Arthritis Clinical Trials)

1. Number of painful joints
2. Number of swollen joints
3. Pain
4. Global disease assessment by the patient
5. Global disease assessment by the physician
6. Acute phase reactants
7. Physical functional capacity
8. Radiologic damage (RA of more than 1 year's evolution)*

*The evaluation of radiographic damage is recommended for studies lasting 1 year or more, although the results of more recent studies have shown that radiographic changes in the hands and feet can be observed in periods of as little as 6 months.

Parameters to Measure the Degree of Inflammatory Activity

- Evaluation of inflammatory activity is recommended by counting the number of painful and swollen joints, assessment of pain, global disease assessment (by patient and by physician), measurement of acute phase reactants, and synthesis of this information using combined activity indices (Disease Activity Score [DAS], Simplified Disease Activity Index [SDAI]). [5, D]

Joint Counts

- The evaluation of the number of painful joint and the number of swollen joints should be performed using validated methods based on counting at least 28 joints. [5, D]

Evaluation of Pain

- Pain should be assessed by the patient him/herself. It is recommended that pain be measured using a horizontal visual analog scale, 10 cm in length, divided by vertical marks into ten equal 1-cm segments. The measurements should be accompanied by numeric descriptors from 0 to 10, with indicators at each end showing no pain (0) and worst pain (10). (see Figure 1 in the original guideline document). [5, D]

Global Assessment of Disease

- A global assessment of disease should be made, from the point of view of both the physician and the patient. For this measurement, the use of a 10 cm horizontal visual analog scale is recommended, with vertical marks dividing it into 10 equal 1 cm segments. The measurements should be accompanied by numeric descriptors from 0 to 10, with "very good" (0) at one end and "very poor" (10) at the other. (see Figures 2 and 3 in the original guideline document). [5, D]

Acute Phase Reactants

- Laboratory tests should include two acute phase reactants (APRs): ESR, and CRP. The behavior of these two APRs is closely related with the inflammatory activity of the disease. [5, D]

Composite Indices of Disease (DAS, SDAI)

The use of composite indices summarizing information on various parameters in a single indicator is a useful and valid procedure in assessing disease activity. This guideline recommends the use of the DAS/DAS28 and/or the SDAI. [5, D]

Classification of Level of Inflammatory Activity

The ACR considers clinical remission to exist when at least five of the six criteria are met for a period of at least 2 months. The clinical utility of this definition is low because it uses two criteria not routinely used in patient evaluation.

Table: American College of Rheumatology (ACR) Criteria* for Clinical Remission of Rheumatoid Arthritis (RA)

1. Morning stiffness absent or not exceeding 15 minutes
2. No fatigue
3. No joint pain in medical history
4. No joint tenderness
5. No soft tissue swelling in joints or tendon sheaths
6. Normal erythrocyte sedimentation rate

* ACR considers clinical remission to occur when at least five of the six criteria are met.

Evaluation of Disability

Physical Disability

- Self-perceived functional disability attributed to the disease should be evaluated with specific, previously validated questionnaires. This

guideline recommends the use of the Health Assessment Questionnaire (HAQ) as a tool for the standard evaluation of disability, due to its wide diffusion, acceptance, and proven metric characteristics. [5, D]

Ability to Work

- RA very frequently causes loss of the ability to work. The panel recommends that this aspect be jointly assessed with the patient to implement strategies that make it possible to continue working as long as possible without prejudice to the patient. [5, D]

Psychological and Social Aspects

- Some psychological aspects such as mood (depression, anxiety) or social support are very important for patients and can affect compliance with treatment and treatment response. The panel recommends keeping these aspects in mind when assessing the need for additional interventions. [5, D]

Evaluation of Structural Damage

Radiologic Indices

- Radiographs of the hands, feet, and chest are recommended in the initial evaluation; hand and foot radiographs should be repeated annually during the first three years of disease evolution and subsequently as deemed necessary. [5, D]

Ultrasonography

- Ultrasound is recommended when the physical examination raises doubts about the existence of signs of inflammatory joints, or when ultrasound detection of synovitis, effusion, or erosions will modify management of the patient's treatment. [5, D]

Magnetic Resonance Imaging (MRI)

- MRI is recommended for the detection of synovitis, effusion, and erosions when this information is considered to be clinically relevant. [5, D]

Evaluation of Prognosis

- The initial and subsequent evaluation of RA patients should include a continuing estimate of disease prognosis. The evaluation of prognosis should take into account sociodemographic factors, genetic markers, disease-dependent factors, treatment-dependent factors, and psychological and social factors. [5, D]

Treatment Evaluation

Objective of RA Treatment

- The objective of treatment of RA is to induce complete remission of the disease [3.c]. In patients with a longer history, the objective of treatment may be to achieve low disease activity. [1b, A]

Treatment-Response Criteria

- Treatment-response criteria should be applied to each patient individually; therefore, they should take into account the change in disease activity and the current degree of activity. [5, D]

ACR Response Criteria

- The ACR criteria do not take current disease status into account; therefore the following modification proposed by the Spanish Society of Rheumatology (SER) is recommended if they are applied. [5,D]
  The ACR criteria for improvement define a dichotomous outcome (response/no response) according to the following criteria:
  - Improvement of 20% or more in the tender joint count and in the swollen joint counts.
  - Improvement of 20% or more in at least three of the following parameters: ESR or CRP, physician global assessment of disease activity, patient global assessment of disease activity, patient pain assessment, physical disability

  The ACR response criteria are likely to be modified in the near future; meanwhile, the following adaptation is proposed: (http://www.ser.es/):
  - Satisfactory response: fulfillment of the ACR20 criteria, fewer than 6 swollen joints, and absence of any patient circumstance that

results in intolerable loss of functional capacity in the opinion of the patient or physician.
- Unsatisfactory response: failure to meet the criteria for satisfactory response.

Subjective Physician Assessment of Disease Activity

- The subjective physician assessment of disease activity is the clinical criterion most commonly used in daily practice. It is not advisable to use it as the only response criterion. [5, D]

Frequency of Check-ups

- RA patients should be followed indefinitely: cases of established RA and in complete disease remission should be evaluated every 6-12 months; those with frequent outbreaks or with persistent activity and those who have recent-onset disease should be assessed "on demand" (in general, every 1-3 months) until remission is achieved or until reaching and maintaining the least possible inflammatory activity. [5, D]

Nursing Consultations

- The active incorporation of nursing staff is recommended from the outset to assist in the evaluation of disease inflammatory activity, facilitate early detection of side effects and comorbidity, and improve health education. [5, D]

Periodic Check-ups and Administration of Questionnaires

- Joint counts and other parameters included in the systematic clinical evaluation of the patient should be carried out in the nursing consultation. [5, D]

Monitoring the Adverse Effects of Disease-Modifying Anti-rheumatic Drugs (DMARDs) and Treatment with Biologics

- It is recommended that adverse treatment effects be monitored in the nursing consultation. The rheumatologist who is responsible for the patient should be informed of any possible adverse effect, whether objective or subjective. [5, D]

Patient Education

- A patient education program should be implemented that includes at least the following aspects: 1) monitoring and control of the adverse effects of DMARDS and biologic treatments; 2) exercise; 3) pain control; 4) joint protection. [5, D]

RA Comorbidity

- The rheumatologist is responsible for controlling the inflammatory process and should monitor RA-associated comorbidity with the support of the primary care physician and with recourse to other specialists when needed. [5, D]

RA Complications

Amyloidosis

- Secondary amyloidosis should be suspected in RA patients who develop proteinuria, renal failure, gastrointestinal symptoms, myocardiopathy and/or hepatomegaly, and in those who have elevated APRs concurrent with little clinical activity. [5, D]
- Treatment should be preventive and should aim to suppress the inflammatory activity of RA. There is no single clear standard for the treatment of established amyloidosis. Several published case series have shown important improvements in proteinuria and renal function in patients with amyloidosis secondary to RA treated with anti-tumor necrosis factor (anti-TNF), which, given its lower toxicity, is a good treatment alternative. [4, C]

Anemia

- Periodic blood cell counts and general liver and kidney function tests are recommended. [5, D]
- Chronic anemia in conjunction with RA does not usually require treatment. Oral iron supplements are not indicated, except in cases of ferropenic anemia. The use of erythropoietin is controversial. [5, D]

Cardiological Complications

- RA-related cardiac involvement should be suspected in the presence of pericardial pain, heart failure, or conduction abnormalities. [5, D]
- Pericarditis should be treated initially with full doses of nonsteroidal anti-inflammatory drugs (NSAIDs) (150 mg/day of indomethacin); if this is not effective, prednisone (1 mg/kg/day); the rare cases of cardiac tamponade should be treated with evacuation by pericardiocentesis. [4,

C]
- In addition to treatment for heart failure, myocarditis requires treatment with high-dose prednisone. [4, C]

Pulmonary Complications

- Pulmonary disease should be suspected if there is pleuritic pain, progressive or recent-onset dyspnea, or hemoptysis. [5, D]
- In the case of pleural involvement, thoracocentesis is recommended to obtain an exudate and rule out other diseases (infection or neoplasia). [5, D]
- Pleural involvement should be treated with full-dose or medium-dose steroids (10-20 mg/day of prednisone). [4, C]
- Rheumatoid nodules do not require treatment in the absence of complications. [5, D]
- Recent-onset (acute) interstitial involvement is treated with prednisone (1-1.5 mg/kg/day). If there is no response, patients may be treated with cyclophosphamide or azathioprine. Bronchiolitis obliterans organizing pneumonia (BOOP) is treated with prednisone (1.5 mg/kg/day). [4, C]

Felty's Syndrome

- Treatment for Felty's syndrome requires comprehensive control of RA inflammatory activity. As a specific measure, the use of filgrastim is recommended when the absolute neutrophil count is lower than 1,000/mm^3 and the patient has a history of severe infections associated with the disease. [5, D]

Secondary Sjögren's Syndrome (SSS)

- There are no specific recommendations for modifying the course of SSS in RA. The recommendations in this guideline include symptomatic treatment of xerophthalmia and xerostomia. Dental and ophthalmological examinations at least every 6 months are recommended. [5, D]

Vasculitis

- Palpable purpura should be treated with full-dose NSAIDs and medium-low doses of prednisone (15-30 mg/day). [4, C]
- Polyarteritis nodosa is treated initially with high-dose steroids (40-120 mg/day of prednisone). If there is no response, cyclophosphamide should be added (2-3 mg/kg/day orally or 0.5-1 g/m^2 in intravenous pulses of 2 to 4 weeks). [4, C]

Comorbidity Not Directly Related with RA

Infections

- Extreme precautions should be exercised in RA patients to prevent infections. Recommended measures include receipt of routine vaccinations, but never with attenuated microorganisms if the patient is receiving immunosuppressive treatment [4, C], avoiding contacts with tuberculosis patients and receiving chemoprophylaxis with isoniazid as needed [2.b, B], and practicing scrupulous dental hygiene. [2.b, B]

Tuberculosis (TB)

The following recommendations of the SER and the Spanish Medicines Agency (AEME in Spanish) have made it possible to reduce the risk of TB activation in patients undergoing anti-TNF treatment to nearly normal levels:

Table: SER and AEME Recommendations to Control the Risk of TB in Patients with Anti-TNF Treatment

Clinical history should include:	History of tuberculosis
	Recent contacts with tuberculosis patients
Should also perform:	Chest radiograph to rule out active tuberculosis or radiographic signs consistent with old tuberculosis infection
	Tuberculin skin test (PPD) (see following table)

SER, *Sociedad Española de Reumatología* (Spanish Rheumatology Society); AEME, *Agencia Española del Medicamento* (Spanish Medicines Agency); TB, tuberculosis; anti-TNF, anti-tumor necrosis factor; PPD, purified protein derivative

Table: SER and AEME Recommendations According to PPD Results

If PPD is positive (induration ≥5 mm at 48-72 hours), patient is considered to have latent tuberculosis infection.
If anergy or induration less than 5 mm is detected, a new tuberculin test (booster) should be performed, 1-2 weeks afterwards, especially in persons over age 50.
If induration is ≥5 mm at 48-72 hours after booster, patient is also considered to have tuberculosis infection.
In individuals vaccinated with BCG it is impossible to know whether a positive PPD is a consequence of the vaccine or indicates latent tuberculosis infection; therefore, the same recommendations should be followed as for those who are not vaccinated.

SER, *Sociedad Española de Reumatología* (Spanish Rheumatology Society); AEME, *Agencia Española del Medicamento* (Spanish Medicines Agency); PPD, purified protein derivative; BCG, Bacille Calmette-Guerin

Cardiovascular Complications

- Individual risk factors for cardiovascular (CV) complications should be identified and treated: age, male sex, highly active arthritis, smoking, arterial hypertension, hypercholesterolemia, and history of CV episode. [1.b, A]

Osteoporosis

- When RA is first diagnosed, the principal risk factors for fracture and loss of bone mass should be analyzed; if any are present, bone densitometry is indicated. [5, D] (See table below).
- The first-line treatment options for osteoporosis are alendronate and risedronate, with cyclic etidronate or calcitonin as alternatives. [5, D]
- Hormone treatment is not indicated. [5, D]

Table: Risk Factors for Osteoporosis

Factors Independent of RA
Age over 65 years
History of fragility fracture after age 40
Body weight less than 58 kg
Fragility fractures in first-degree relatives
Smoking
Early menopause
Prolonged amenorrhea
Male hypogonadism
Other predisposing diseases for osteoporosis
Factors Associated with RA or Its Treatment
Active disease
HAQ >1.25
Treatment with glucocorticoids: >7.5 mg/d for more than 3 months, continuous treatment with >2.5 mg/d, or cumulative dose over 30 g.

RA, rheumatoid arthritis; HAQ, Health Assessment Questionnaire

Neoplasias

- Discontinuation of all tobacco use is indicated in all RA patients. [5, D]
- Anti-TNFs are not recommended in patients with a personal history of lymphoma. [4, C]
- In patients with a personal history of lymphoma, the risk/benefit ratio should be carefully evaluated before deciding to use a tumor necrosis factor (TNF) antagonist. [5, D]
- History of a malignant solid tumor in the last 5 years is a contraindication for the use of anti-TNF agents. [5, D]
- If there is history of a malignant solid tumor longer than 5 years previously, the physician should consult the specialist in oncology about the biopathology of the tumor. [5, D]
- An RA patient who develops a tumor should discontinue all DMARDs except antimalarials, gold salts, and sulfasalazine (SSZ). [5, D]

Pharmacological Treatment

Pharmacological Treatment of Recent-Onset Rheumatoid Arthritis

- All RA patients should be treated with a DMARD as soon as the clinical diagnosis of the disease is established, regardless of whether they meet the ACR classification criteria. [1a, A]
- The initial treatment recommended in all patients who have not been previously treated with a DMARD is methotrexate (MTX), due to its excellent safety and efficacy profile. [1a, A]
- For optimal use of MTX as a remission-inducing agent in early RA, a rapid step-up dose to 20 or 25 mg weekly is recommended by 3-4 months after initiation of MTX. In refractory cases, MTX bioavailability should be assured by subcutaneous administration. [1a, A]
- Nonetheless, given the clinical complexity of RA, the panel considers that, in some clinical situations, initial DMARD treatment may consist of using other drugs that have also been shown to control signs and symptoms of the disease and to delay radiologic progression. [5, D]
- In early RA with no markers of poor outcome (radiologic erosions, RF, anti-CCP antibodies, absence of extra-articular disease, HAQ over 1, or high inflammatory burden), it is acceptable to begin treatment with other DMARDs that have a lower toxicity profile or are easier to monitor for side effects; typical examples of these are the antimalarials or SSZ. [5, D]
- In early RA that is expected to be especially incapacitating due to characteristics of the disease, the patient, or the patient's type of employment, initial combination therapy with MTX and an anti-TNF agent may be indicated; the objective of this treatment is to induce rapid remission and try to withdraw the anti-TNF agent and maintain RA remission with MTX in monotherapy. [5, D]

Refer to Table 18 in the original guideline document for recommended doses and commercial names of the principal DMARDs.

Changes in Treatment

- Therapeutic failure or toxicity should be evaluated no later than 3 months after starting therapy; if necessary, a change in treatment should be considered. The objective of treatment should be clinical remission of disease [3b, C] or, when this is not possible, low disease activity [1b, A].
- If response to MTX is unsatisfactory after reaching the maximum dosage and assuring the bioavailability of the agent, the panel recommends the use of leflunomide (LEF) or SSZ or an anti-TNF agent as the second step in the treatment ladder, either replacing or in addition to MTX. If MTX toxicity is such as to oblige its withdrawal, the panel recommends using LEF or SSZ or an anti-TNF agent as the second step on the treatment ladder. [5, D]
- In patients for whom the previously described guidelines are not useful due to lack of efficacy, toxicity, or other reasons, use of any of the DMARDs, combinations, or other biologic agents is recommended; if these fail, experimental treatments should be tried. [5, D]
- Other biologic agents such as abatacept (ABT) or rituximab (RTX) are reasonable alternatives in patients who have not responded to or who have experienced toxicity with one or more anti-TNF agents.

Treatment with Glucocorticoids

- In recent-onset RA the use of low-dose oral glucocorticoids (GC) is the recommended disease-modifying therapy, always in combination with a DMARD. [1.b, A]
- In RA of long duration, the use of low-dose oral glucocorticoids is recommended as anti-inflammatory therapy for symptom control while waiting for the DMARDs to take effect. [5, D]
- Given the association between glucocorticoid use and rapid loss of bone mass, it should at a minimum be used jointly with Vitamin D and calcium, and other preventive treatments for osteoporosis should be evaluated (see section III.3.2.c. in the original guideline document) if treatment is expected to exceed 3 months. [5, D]
    - The use of intra-articular glucocorticoids is essential in the management of joints that are persistently inflamed despite good therapeutic response to the DMARD regimen.

Treatment with NSAIDs

- The NSAIDs are used to modify the symptoms of RA. The use of NSAIDs is recommended at disease onset, when a new DMARD is introduced, and occasionally when uncontrolled isolated symptoms persist despite good response to a DMARD. [5, D]. The need for continuous use of NSAIDs in a patient with RA should be interpreted as inadequate control of inflammatory activity and should, therefore, lead to reassessment of the DMARD regimen. [5, D]
- All NSAIDs should be used at the full dose for at least 1 week before considering the treatment to have failed. Once symptoms have been controlled, the minimum effective dose should be used. [5, D]
- There is no evidence that some NSAIDs are better than others; therefore the one that best fits the patient characteristics should be used. [5, D]
- The need for co-treatment with gastric protectors should be evaluated on an individual basis. [5, D]

Treatment for Pain

- Analgesics are indicated to control pain. If there is no response, surgical treatment can be considered, especially to restore function and mobility. [5, D]

Treatment of RA in Special Situations

Elderly Patients

Monitoring Kidney and Liver Function

- Kidney and liver function should be monitored in elderly patients, and the dosage intervals of the drugs eliminated by these routes should be adapted accordingly. [5, D]

Monitoring Adverse Effects and Drug Interactions

- The possible appearance of adverse effects and interactions among drugs taken regularly should be monitored in elderly patients. [5, D]

Pregnancy and Breastfeeding

Prevention

- Women of childbearing age should be informed of the possible effects of RA on pregnancy, in particular, because of the implications for treatment. [5, D]

Drug Management during Pregnancy and Breastfeeding

- The use of NSAIDs during pregnancy and breastfeeding should be avoided insofar as possible. Corticosteroids can be used under controlled conditions. DMARDs should be managed on an individual basis, and should preferably be continued during pregnancy. [5, D]

Table 25 in the original guideline document shows the considerations to be taken into account with regard to use of anti-rheumatic drugs during pregnancy and breastfeeding.

For information about the safety of pharmacological treatments, including recommendations for monitoring, see Section VI and Table 26 in the original guideline document.

Other Treatments

Intra-articular Treatment

Types of Intra-articular Treatment

- The recommended local treatment of choice is intra-articular infiltration with slow-release steroids. When steroid infiltrations have failed (three consecutive infiltrations 4 weeks apart), isotopic synovialitis or chemical synovitis with osmic acid can be considered. Before starting local treatment, the presence of infection should be reasonably ruled out. [5, D]

Rehabilitation in Rheumatoid Arthritis

Non-pharmacological Interventions

Therapeutic Exercise

- From the time of diagnosis a program of aerobic physical exercise is recommended. It should initially be supervised to adapt it to the individual's level of physical preparation and the specific joint and extra-articular circumstances stemming from the disease and comorbidities. [1.a, A]

Physical Treatments (Passive Modalities)

- Low level laser therapy and transcutaneous electrical nerve stimulation (TENS), used alone and independently, are effective in reducing pain in the short term (TENS has the advantage of easy application with portable units that can be used at home). [1.a, A]
- The combination of paraffin (thermotherapy) and active exercises also appears to be effective against pain. Data on ultrasound, muscular electrostimulation, and magnetotherapy remain insufficient to recommend them for routine use, but they should be considered in selected cases that do not respond to other alternatives. The application of thermotherapy alone and the local application of cold do not appear to offer any clinical benefit. [2.b, B]

Integral Occupational Therapy

- In patients with important functional limitations, usually those with advanced disease, a lasting improvement has been observed. [1.b, A]

Joint Protection and Energy Conservation Programs

- In advanced phases of RA it is useful to instruct the patient about rules for joint protection. Teaching strategies to conserve energy is indicated only in patients in whom fatigue is an important symptom. [4, C]

Assistive Devices

- The use of assistive devices for important tasks should be evaluated in RA patients who have difficulties carrying out basic or instrumental activities of daily living due to weakness or lack of manual dexterity (who do not improve with an exercise program), or due to pain (that is not controlled with other therapies). [5, D]

Orthotics

Splints or Upper Limb Orthotics

- In periods of active inflammation (with the main objective of avoiding pain and reducing inflammation), static orthotics can be used (at first during the whole day and later only at night). If the patient has functional problems these can be combined during the day (part time) with functional orthotics adapted to the specific problem and to the anatomical region interfering with function. [4, C]
- Their efficacy should be evaluated periodically, and orthotics that do not meet expectations should be rejected. [5, D]

Lower Limb Orthotics

- Pain of the forefoot can be improved with hard and soft orthotics. Hard orthotics improve pain in the hindfoot in the initial phase of the disease. Use of a special model can prevent the development and progression of hallux valgus. Shoes with special widths improve the results. [1.a, A]
- Studies of orthotics are highly heterogeneous, and it is not possible to establish which type of orthotic is the most appropriate for each type of involvement. [5, D]

Balneotherapy

- Balneotherapy can be recommended in cases of polyarticular involvement without active disease, where other more accessible therapies have been ineffective. [2.b, B]

Combination Treatments. Multidisciplinary Approaches

- It is important that all professionals who participate in the treatment of the RA patient have a coordinated approach focusing on specific problems, with appropriate assessment of the effects of interventions. [5, D]

Surgical Treatment in RA*

- Before performing surgical treatment, several factors should be considered: bone quality, the patient's preferences and level of motivation, estimation of the extent to which disease progression can be modified by surgery, and estimation of the degree to which surgical treatment

can reconstruct joint function and improve the patient's independence. [5, D]
- The joint prosthesis is the most effective surgical measure to halt the progressive loss of functional capacity. Joint replacement, in whatever joint, should be performed before irreversible deformities become established. [5, D]

Note: *This section has not been updated since GUIPCAR-2001.

Definitions:

Levels of Evidence

See Table 1, "Levels of Evidence, Oxford Centre for Evidence-Based Medicine," and the accompanying explanatory notes in the original guideline document.

Grades of Recommendation*

A. Based on the results of consistent level 1 studies
B. Based on the results of consistent level 2 or 3 studies or on extrapolations** from level 1 studies
C. Based on the results of level 4 studies or on extrapolations** from level 2 or 3 studies
D. Based on the results of level 5 studies or on troublingly inconsistent or inconclusive studies of any level

*See Table 1 in the original guideline document for an explanation of the levels of evidence according to the Oxford Classification for Evidence-Based Medicine

**"Extrapolations" are where data is used in a situation which has potentially clinically important differences than the original study situation.

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

Rheumatoid arthritis (RA)

Other Disease/Condition(s) Addressed

- Cardiovascular complications
- Neoplasia
- Osteoporosis
- Tuberculosis

Guideline Category

Counseling

Diagnosis

Evaluation

Management

Rehabilitation

Risk Assessment

Treatment

Clinical Specialty

Family Practice

Geriatrics

Internal Medicine

Physical Medicine and Rehabilitation

Rheumatology

Surgery

Intended Users

Advanced Practice Nurses

Nurses

Occupational Therapists

Physical Therapists

Physician Assistants

Physicians

Psychologists/Non-physician Behavioral Health Clinicians

Social Workers

Guideline Objective(s)

To update the 2007 Clinical Practice Guideline for the Management of Rheumatoid Arthritis in Spain

Target Population

Adult patients with rheumatoid arthritis living in Spain

Interventions and Practices Considered

Diagnosis

1. Referral of suspected cases of rheumatoid arthritis from primary care physicians to rheumatologists in a timely fashion
2. Use of American College of Rheumatology (ACR) classification criteria
3. Measurement of rheumatoid factor and anti-cyclic citrullinated peptide (anti-CCP) antibodies

Evaluation

1. Clinical history and physical examination
2. Blood tests including complete blood count, erythrocyte sedimentation rate (ESR), C-reactive protein, rheumatoid factor, anti-CCP, liver biochemistry and serology, and renal function
3. Urinalysis
4. Evaluation of inflammatory activity

5. Patient assessment of pain, using a horizontal visual analog scale
6. Global assessment of disease by both physician and patient
7. Composite indices of disease, including Disease Score Activity (DAS) and/or the Simplified Disease Activity Index (SDAI)
8. Evaluation of functional disability (e.g., use of Health Assessment Questionnaire [HAQ])
    - Physical disability
    - Ability to work
    - Psychological and social aspects
9. Evaluation of structural damage
    - Radiographs of the hands, feet, and chest
    - Ultrasonography
    - Magnetic resonance imaging (MRI)
10. Evaluation of disease prognosis taking into account sociodemographic factors, genetic markers, disease-dependent factors, treatment-dependent factors, and psychosocial factors
11. Treatment evaluation that includes patient education and monitoring adverse effects and comorbidities

Treatment

Pharmacologic Treatment

1. Disease-modifying antirheumatic drugs (DMARDs) (e.g., methotrexate) and biologicals
2. Changes in treatment due to therapeutic failure or toxicity
    - Substitution or addition of new DMARD
    - Dosage modification
3. Glucocorticosteroids
4. Nonsteroidal anti-inflammatory drugs (NSAIDs)
5. Treatment for pain (analgesics or surgical treatment)
6. Treatment of rheumatoid arthritis in special populations, including the elderly and during pregnancy and breastfeeding

Other Treatments

1. Local therapy
    - Intra-articular steroid injection
    - Radioisotopic synovectomy
    - Chemical synovectomy
2. Rehabilitative therapy
    - Therapeutic exercise
    - Low level laser therapy and transcutaneous nerve stimulation (TENS)
    - Combination of paraffin (thermotherapy) and active exercise
    - Joint protection and energy conservation programs
    - Assistive devices
    - Orthotics
    - Balneotherapy
    - Occupational therapy
3. Surgical treatment, including joint replacement

Evaluation for Response and Follow-up

1. Use of ACR criteria for clinical remission
2. Use of European League Against Rheumatism (EULAR) criteria for clinical remission
3. Subjective physician assessment of disease activity
4. Nursing consultation
5. Monitoring of adverse effects of DMARDs and biologicals
6. Patient education programs on monitoring and control of adverse effects of DMARDs and biologic treatments, exercise, pain control, and joint protection
7. Follow-up (based on longitudinal monitoring of parameters used in the initial evaluation)
8. Monitoring and treatment of comorbidities and complications

Major Outcomes Considered

- Predictive value and prognostic utility of diagnostic tests
- Symptom relief (changes in pain score, stiffness, inflammation, number of swollen/tender joints)
- Joint damage (assessed radiologically)
- Disability (e.g., ability to work, use of assistive devices)
- Quality of life (e.g., scores on health assessment questionnaires, activities of daily living)
- Rate of disease progression
- Clinical remission rate
- Adverse drug effects
- Cost and cost-effectiveness of diagnostic or treatment interventions
- Safety of diagnostic or treatment interventions
- Mortality rate

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

Review of the Evidence

Summary

The group of reviewers of the Spanish Society of Rheumatology performed the reviews updating the previous GUIPCAR systematic literature reviews. Specifically, the search strategy was reproduced and improved, adding the drugs approved following the publication of the first version of the guide and following the same criteria for study selection. All was carried out by three reviewers. The data extraction was performed by two of them working independently. After the information was collected, the third reviewer introduced all the data in the Review Manager software program and produced the systematic review and meta-analysis, where appropriate.

Criteria for Study Selection

Types of Studies

Inclusion criteria:

- All randomized controlled trials (RCTs) comparing a biologic with placebo, with methotrexate, or their combination with a disease-modifying anti-rheumatic drug (DMARD) versus the biologic in monotherapy
- All the RCTs on DMARDs that had not been included in GUIPCAR
- Cohorts of high quality in the absence of RCTs for specific questions

Types of Participants

Patients over 16 years of age diagnosed with rheumatoid arthritis (RA) according to the 1987 American College of Rheumatology (ACR) criteria, regardless of previous disease duration. By design, the patients normally have active disease, as evinced by at least two of the following parameters: number of painful joints, number of swollen joints, morning stiffness, or elevated erythrocyte sedimentation rate or C-reactive protein.

Types of Interventions

All efficacy studies of the following drugs were included:

- Subcutaneous (SC) etanercept, intravenous (IV) infliximab, SC adalimumab, SC anakinra, IV rituximab, IV toxcilizumab, SC golimumab, SC abatacept, or their original molecules either in monotherapy or in combination with a DMARD, primarily oral or SC methotrexate. Placebo or active treatments such as oral or SC methotrexate or other DMARD were accepted as the control group.
- Methotrexate, leflunomide, cyclosporin, etc., and any other DMARD

Types of Outcome Measurements

RCTs with the following outcomes were included:

1. Efficacy:
    I. Activity: ACR 20%, 50% and 70%; EULAR (European Leagues Against Rheumatism) response, differences in Disease Activity Score (DAS) (28 or complete)
    II. Quality of life: differences in Health Assessment Questionnaire (HAQ), % improvement in HAQ
    III. Radiologic progression: differences in the Sharp index, differences in the modified van der Heijde index or in Larsen's index
2. Safety: difference in percentage of adverse effects

Search Strategy to Identify Studies

Electronic Search

An improved search strategy used in the original GUIPCAR was performed, updated to 2011. Searches were made for randomized controlled clinical trials (RCCTs) in the following databases:

1. MEDLINE (July 2011)
    i. From 2006, with all drugs included
    ii. Up to 1999, with drugs not included in GUIPCAR (adalimumab, abatacept, rituximab, and anakinra)
2. EMBASE (July 2011)
    i. From 2006, with all drugs included
    ii. Up to 1999, with drugs not included in GUIPCAR (adalimumab, abatacept, rituximab, and anakinra)
3. Cochrane Library (July 2011)
4. *Índice Médico Español* (IME)
5. Cochrane Central and other Cochrane groups (July 2011)

See the original guideline document for details of the search strategies.

Manual Search

Secondary searches were made using the reference lists of the selected articles.

Study Selection

Two reviewers carried out the initial study search and selection in two steps: selection by title and selection by abstract. Uncertainties during the selection process were discussed with a third reviewer. This investigator subsequently selected the articles by type of intervention and obtained the complete text of the selected articles without an abstract, and of the studies selected by abstract.

Number of Source Documents

Not stated

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

See Table 1, "Levels of Evidence, Oxford Centre for Evidence-Based Medicine," and the accompanying explanatory notes in the original guideline document.

Methods Used to Analyze the Evidence

Meta-Analysis

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

Review Group of the Spanish Society of Rheumatology

The review of the evidence was carried out by the review group of the Spanish Society of Rheumatology (SER). This group is composed of trained rheumatologists with experience in systematic literature reviews, whose main interest is the use and dissemination of the tools of so-called Evidence-Based Medicine within the community of Spanish rheumatologists.

This group has been enriched by the persons who attended the seven courses on evaluation of the evidence that have been held annually or semi-annually since 2003 in the Spanish Society of Rheumatology. A selection was made from the most capable students interested in conducting systematic literature reviews.

The group is currently made up of 24 rheumatologists who have worked on numerous systematic reviews (available at the SER website under "Grupos de Trabajo": http://www.ser.es/investigacion/Grupo_Trabajo/RBE.php).

The methodology used is based on that proposed by the Cochrane Collaboration.

Review Methods

Data Extraction

Two reviewers independently extracted the descriptive data, results, and estimations of the studies meeting the selection criteria, using a standardized form. Disagreements were resolved by review of a third reviewer. They also carried out secondary searches for studies by reviewing the references of the selected articles.

Data Analysis

The qualitative variables were extracted as absolute values, and were divided by the number of patients in the corresponding group (n/N), and the quantitative variables, as the mean and standard deviation in each group. If the article only contained confidence intervals for the mean, but not the standard deviation, the latter was calculate based on the former.

When the outcome measures and the trials were homogeneous, the possibility of performing meta-analysis was considered. The efficacy outcomes of the trials were combined using random effects models to calculate the difference in means (MD) for quantitative variables or the relative risks (RR) for qualitative variables, with their 95% confidence intervals (CI). Safety outcomes were combined using fixed effects models to calculate the RR with its 95% CI. Heterogeneity was studied using the chi-square statistic included in the RevMan program for review and meta-analysis (version 4.2.8), which was used for the review. In exploring heterogeneity, different sensitivity analyses were used whenever necessary: a) using only intention-to-treat analysis, and b) by financing of the clinical trials. Study quality and patient type were also used in exploring heterogeneity.

When meta-analysis was not possible because the trials could not be combined, the individual outcomes of each study are summarized in qualitative form.

Application of the Reviews

The reviews were sent to the panel of experts for their evaluation before the date on which they had to formulate their recommendations for their corresponding section. Thus, the experts could base their recommendations on the synthesis of the available evidence.

The reviews were used to rank the level of evidence for the GUIPCAR_2011 recommendations, in accordance with the Levels of Evidence of the Oxford Centre for Evidence-Based Medicine (after the March 2009 modification).

Methods Used to Formulate the Recommendations

Description of Methods Used to Formulate the Recommendations

The Spanish Society of Rheumatology (Spanish acronym SER) named a panel of 18 experts to update GUIPCAR (*Guía de práctica clínica de la rheumatoid arthritis* [Rheumatoid Arthritis Clinical Practice Guideline]), made up predominantly of persons who had participated in writing the guideline in 2001. Most of the expert panel members are rheumatologists, although the group also included a primary care physician, a nurse, and two physical therapists. In addition, a group of reviewers carried out the update of the scientific evidence. The company TAISS (*Técnicas Avanzadas de Investigación en Servicios de Salud*) was responsible for coordinating the work and editing the updated version of GUIPCAR (GUIPCAR_2007).

Four methodological phases of the project can be distinguished:

- Preliminary phase: Structure of GUIPCAR_2011 and task assignment
- Review of the evidence
- Drafting the contents of GUIPCAR_2011
- Editing GUIPCAR_2011

Preliminary Phase: Structure of GUIPCAR_2011 and Task Assignment

In March 2011 a meeting was held with the experts responsible for drafting GUIPCAR_2011 and the SER investigators. At this meeting it was decided that GUIPCAR_2011 would be organized in 8 chapters: I. Methodology; II. Background; III. Diagnosis; IV. Evaluation; V. Pharmacological treatment; VI. Safety of pharmacological treatment; VII. Other treatments; and VIII. Management. In drafting GUIPCAR_2011 the longest chapters were separated into sections. The drafting of each chapter or section was assigned to a working team made up of various panelists (from one to three), so that each panelist was part of at least two teams, except for the physical therapists, the primary care physician and the nurse, who were assigned a single chapter or section directly related with their specialty (Other treatments; Nursing diagnosis and consultation, respectively).

The length of the literature review was also decided at this meeting, and the experts were offered the possibility of formulating research questions for the reviewers to be answered by the corresponding literature review. Finally, a working calendar was established and responsibilities were assigned.

Each working team developed the outline for the contents of the section or chapter to which it had been assigned. TAISS coordinated the receipt of all the contents and their incorporation into a single document, which was circulated to the entire group of experts for approval.

Drafting the Contents of GUIPCAR_2011

With the support of the systematic literature review results, each team wrote the assigned chapter or section of GUIPCAR_2011 and formulated a series of provisional recommendations. The text produced was sent to research unit of the SER, which edited a first draft of GUIPCAR_2011 and circulated it to the group of experts.

The group of experts and SER investigators met in September 2011 to discuss the preliminary contents and recommendations. At this meeting some modifications to the text were proposed, and these were introduced by the corresponding team. The SER investigators again edited the manuscript which was resubmitted for the consideration of the group of experts to make the final review.

Editing GUIPCAR_2011

The documents produced by the different teams of experts were combined into a single document, and given a uniform style. The most important information, from the practical point of view for the physician, was extracted and used to write the Rapid Guideline. Finally, a list of the main recommendations was produced, with a description of the level of scientific evidence on which each is based, according to the Oxford classification for Evidence-Based Medicine, and the strength of the recommendation (see the "Rating Scheme for the Strength of the Evidence" and the "Rating Scheme for the Strength of the Recommendations" fields).

Rating Scheme for the Strength of the Recommendations

Grades of Recommendation*

A. Based on the results of consistent level 1 studies
B. Based on the results of consistent level 2 or 3 studies or on extrapolations** from level 1 studies
C. Based on the results of level 4 studies or on extrapolations** from level 2 or 3 studies
D. Based on the results of level 5 studies or on troublingly inconsistent or inconclusive studies of any level

*See Table 1 in the original guideline document for an explanation of the levels of evidence according to the Oxford Classification for Evidence-Based Medicine

**"Extrapolations" are where data is used in a situation which has potentially clinically important differences than the original study situation.

Cost Analysis

The guideline developers reviewed published cost analyses.

Method of Guideline Validation

Not stated

Description of Method of Guideline Validation

Not applicable

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified and graded for each recommendation (see the "Major Recommendations" field.)

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Appropriate management of rheumatoid arthritis, which might:

- Provide symptom relief (pain, stiffness, inflammation)
- Reduce joint damage
- Decrease disability
- Maintain or improve quality of life
- Slow disease progression

Potential Harms

- The most frequent adverse effects associated with pharmacologic treatment of rheumatoid arthritis (RA), along with recommendations for monitoring, are summarized in Table 26 in the original guideline document.
- Treatment with disease-modifying anti-rheumatic drugs (DMARDs) can have negative consequences on pregnancy, the fetus, and breastfeeding. Thus, women of childbearing age should know the risk so they can act accordingly. See section V.1.4. of the original guideline document for additional information.
- Adverse drug effects have traditionally been considered more frequent in elderly individuals, although little information is available about most drugs in this age group, including those used in RA patients. The lack of data is due to the frequent exclusion of extreme age groups in

clinical trials. For this reason, unexpected side effects are not uncommon in individuals with late onset RA, once the drugs have come into generalized use.
- In general, elderly patients have more than one disease and need treatment with multiple drugs. This means there is an increased probability of drug interactions and contributes to a larger number of side effects. The use of multiple drugs in elderly patients is often accompanied by lack of treatment compliance, which is estimated at 10 percent.
- The DMARDs and the immunosuppressors have a similar efficacy and safety profile in young and old individuals, although, for the reasons mentioned above, toxicity should be monitored more closely in the elderly.

Contraindications

Contraindications

Contraindications to use of pharmacological treatments for rheumatoid arthritis can be found in Chapter VI of the original guideline document.

Implementation of the Guideline

Description of Implementation Strategy

Chapter VIII of the original guideline document includes a series of indicators for rheumatoid arthritis (RA) management which can be used to help analyze and compare different Units or Services in terms of quality, as well as to evaluate strategies or programs implemented to improve the detection, referral, and speed of diagnosis and treatment of RA patients. These indicators are based on the time elapsed between different stages of the process of care and on quality indicators based on the proportion of RA patients who are managed appropriately.

Implementation Tools

Audit Criteria/Indicators

Chart Documentation/Checklists/Forms

Foreign Language Translations

Quick Reference Guides/Physician Guides

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Getting Better

Living with Illness

IOM Domain

Effectiveness

Patient-centeredness

Identifying Information and Availability

Bibliographic Source(s)

GUIPCAR Group. Update of the clinical practice guideline for the management of rheumatoid arthritis in Spain. Madrid (Spain): Spanish Society of Rheumatology; 2011 Dec. 367 p.

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2001 (revised 2011 Dec)

Guideline Developer(s)

Advanced Research Techniques in the Health Services - For Profit Research Organization

Spanish Society of Rheumatology - Medical Specialty Society

Guideline Developer Comment

This guideline was an initiative of the Spanish Society of Rheumatology. The following institutions collaborated in carrying out this initiative:

Spanish Society of Rheumatology (Sociedad Española de Reumatología - SER). The SER promoted the idea for this guideline, chose the research group to develop it, helped select the panel of experts, sponsored its development, and presented the project to the financing organization.

Health Services Research Unit (Unidad de Investigación en Servicios de Salud - UISS). When the SER decided to produce the guideline in late 1998, the Society proposed that it be developed by the UISS. At that time the UISS was a research unit within the Carlos III Health Institute (ISCIII). The UISS began to develop the guideline, but organizational changes in the ISCIII took place at the end of 2000. The UISS then became a private company with the name of TAISS, part of whose research staff came from the UISS.

Ignacio de Mercado Foundation (Fundación Ignacio de Mercado - FIdeM) for research and education in the health services. The FIdeM contracted project personnel who were not on the staff of the UISS.

Advanced Research Techniques in the Health Services (Técnicas Avanzadas de Investigación en Servicios de Salud, S.L. - TAISS). TAISS is a company devoted to producing knowledge to improve decision making in the health sector at the macro (policy) level, as well as at the meso (management) and micro (physician-patient) levels. Its research staff came from the UISS. All the investigators who participated in the project at its inception have continued to work on it.

Novartis. Novartis is the organization that financed the development of this guideline. It also oversaw each project activity and, together with the SER, monitored project tasks to ensure they were carried out in a correct and timely fashion.

Source(s) of Funding

The only funding provided was from Pfizer, to cover the expense of translating the document into English.

Guideline Committee

Clinical Practice Guideline for the Management of Rheumatoid Arthritis in Spain Expert Panel

Composition of Group That Authored the Guideline

Expert Panel Members: Jose Luis Andreu Sánchez, rheumatologist, Hospital Universitario Puerta de Hierro de Madrid; Alejandro Balsa, rheumatologist, Hospital Universitario La Paz, Madrid; Enrique Batlle Gualda, rheumatologist, Hospital General Universitario de Alicante, Alicante; Federico Díaz González, rheumatologist, Hospital Universitario de Canarias, Santa Cruz de Tenerife; Ángel Elena Ibáñez, rheumatologist, Hospital San Millán-San Pedro de la Rioja (Logroño); Mariano Tomás Flórez García, occupational therapist, Fundación Hospital Alcorcón, Madrid; Fernando García Pérez, occupational therapist, Fundación Hospital Alcorcón, Madrid; Núria Guañabens, rheumatologist, Hospital Clínic de Barcelona; César Hernández García, rheumatologist, Hospital Clínico San Carlos, Madrid; Mª Victoria Irigoyen Oyarzábal, rheumatologist, Hospital General Carlos Haya, Málaga; Jose Luis Marenco de la Fuente, rheumatologist, Hospital Universitario de Valme, Sevilla; Víctor Manuel Martínez Tabeada, rheumatologist, Hospital Universitario Marqués de Valdecilla, Santander; José María Salazar Vallinas, rheumatologist, Hospital Regional Universitario Infanta Cristina, Badajoz; Alejandro Tejedor Varillas, Specialist in Family and Community Medicine, Centro de Salud "Las Ciudades" de Getafe, Madrid; Juana de la Torre Aboki, nurse, Hospital General Universitario de Alicante

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Reviewers: Lydia Abásolo Alcázar, rheumatologist, Hospital Clínico de San Carlos, Madrid; Cayetano Alegre de Miquel, rheumatologist, Hospital Universitario Vall d'Hebron, Barcelona; Eugenio Chamizo Carmona, rheumatologist, General Hospital of Merida; Antonio Fernandez Nebro, rheumatologist, Carlos Haya Hospital, Malaga; Maria Rosa Gonzalez Crespo, Rheumatology, Hospital Doce de Octubre, Madrid; Miguel Angel Hernandez Abad, rheumatologist, Hospital Virgen del Puerto, Caceres; Blanca Hernandez Cruz, Rheumatology, Hospital Virgen Macarena, Seville; Jesús Maese, rheumatologist, Madrid; Jose de la Mata Llord, rheumatologist, Hospital de la Zarzuela, Aravaca; Esteban Mazzucchelli, rheumatologist, Fundación Hospital Alcorcón, Madrid; Santiago Munoz, rheumatologist, Hospital La Paz, Madrid; M Betina Nishishinya, rheumatologist, Hospital de la Santa Creu i Sant Pau, Barcelona; Ana Ortiz García, Rheumatology, Hospital de La Princesa, Madrid; Claudia A. Pereda Testa, rheumatologist, Clínica Mediterráneo, Almería

Financial Disclosures/Conflicts of Interest

A detailed list of conflicts of interest is provided in chapter X of the original guideline document.

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: GUIPCAR Group. Clinical practice guideline for the management of rheumatoid arthritis in Spain. Madrid: Spanish Society of Rheumatology; 2007 Mar. 301 p. [1260 references]

Guideline Availability

Electronic copies: Available from the Spanish Society of Rheumatology Web site .

Print copies (Spanish): Available from the Spanish Society of Rheumatology. C/Marqués del Duero, 5 - 1st floor, 28001 Madrid, Spain; Telephone: +34 91 5767799; Fax: +34 91 5781133; e-mail: ser@ser.es.

Availability of Companion Documents

The following are available:

- Quick reference guide (Spanish). Madrid (Spain): Spanish Society of Rheumatology; 2007. 18 p. Available from the Spanish Society of Rheumatology Web site .

- Recommendations for rheumatoid arthritis (Spanish). Madrid: Spanish Society of Rheumatology; 2007. 8 p. Available from the Spanish Society of Rheumatology Web site .

Print copies (Spanish): Available from the Spanish Society of Rheumatology. C/Marqués del Duero, 5 - 1st floor, 28001 Madrid, Spain; Telephone: +34 91 5767799; Fax: +34 91 5781133; e-mail: ser@ser.es.

Additionally, a series of indicators for rheumatoid arthritis (RA) management and a set of data collection instruments for parameters used in initial evaluation and monitoring of RA patients are available in the original guideline document .

Patient Resources

None available

NGC Status

This NGC summary was completed by ECRI on June 12, 2003. The information was verified by the guideline developer on June 24, 2003. This summary was updated by ECRI on January 12, 2005 following the release of a public health advisory from the U.S. Food and Drug Administration regarding the use of some non-steroidal anti-inflammatory drug products. This summary was updated on April 15, 2005 following the withdrawal of Bextra (valdecoxib) from the market and the release of heightened warnings for Celebrex (celecoxib) and other nonselective nonsteroidal anti-inflammatory drugs (NSAIDs). This summary was updated by ECRI on June 16, 2005, following the U.S. Food and Drug Administration advisory on COX-2 selective and non-selective non-steroidal anti-inflammatory drugs (NSAIDs). This summary was updated by ECRI Institute on August 6, 2009. The updated information was verified by the guideline developer on August 14, 2009. This summary was updated by ECRI Institute on April 1, 2010 following the U.S. Food and Drug Administration advisory on Erythropoiesis-Stimulating Agents (ESAs). This summary was updated by ECRI Institute on July 27, 2010 following the U.S. Food and Drug Administration advisory on Arava (leflunomide). This summary was updated by ECRI Institute on December 10, 2010 following the U.S. Food and Drug Administration (FDA) advisory on Bisphosphonates. This summary was updated by ECRI Institute on October 12, 2011 following the U.S. Food and Drug Administration (FDA) advisory on Tumor Necrosis Factor-alpha (TNFα) Blockers. This NGC summary was updated by ECRI Institute on July 6, 2012. The updated information was verified by the guideline developer on July 30, 2012. This summary was updated by ECRI Institute on November 21, 2013 following the U.S. Food and Drug Administration advisory on Arzerra (ofatumumab) and Rituxan (rituximab). This summary was updated by ECRI Institute on September 18, 2015 following the U.S. Food and Drug Administration advisory on non-aspirin nonsteroidal anti-inflammatory drugs (NSAIDs).

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